UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,600	09/15/1999	ALAN BERRY	3161-18-PUS	5327

22442 7590 03/24/2004

SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	28

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/341,600	BERRY ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 40-70 are under consideration in this Office Action. Rejections stated in the previous Office Action have been withdrawn. New rejections and new grounds of rejection are presented in the instant Office Action.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 40-47, 51, 53-70 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 9, 13-15, 26-33, 37-39, and 50 of U.S. Patent No.6,372,457. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons:

The method of the instant application uses any nucleic acid encoding any glucosamine-6-phosphate synthase from any biological source while the method of in U.S. Patent No.6,372,457 is identical to the method of the instant application except that the method in U.S. Patent No.6,372,457 uses a nucleic acid encoding glucosamine-6-phosphate synthase from *E.coli*. The scope of the method of the instant application encompasses a genus of nucleic acids encoding glucosamine-6-phosphate synthases from many biological sources and the said genus includes a nucleic acid encoding glucosamine-6-phosphate synthase from *E.coli* which is recited in the method claims of U.S. Patent No.6,372,457. Thus, allowance of the method claims of the instant application would improperly extend the "right to exclude" already granted in U.S. Patent No.6,372,457.

Claim Rejections - 35 U.S.C. § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 40-70 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 40-70, as written, do not sufficiently distinguish over nucleic acids, proteins, cells, or antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "transformed microorganism" or "recombinant microorganism". See MPEP 2105.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 40-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a glucosamine-6-phosphate synthase having the amino acid residue at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 replaced with another amino acid residue where the glucosamine-6-phosphate synthase has increased activity compared to a wild-type glucosamine-6-phosphate synthase, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' arguments filed January 19, 2001 (paper no. 14), have been fully considered but they are not persuasive. Applicants argue that the specification is enabling and that it is not necessary to have prior knowledge of the amino acid sequence of the claimed glucosamine-6-

phosphate synthase in order to obtain mutants with the desired property of increased enzyme activity.

The nature and breadth of the claims encompass any microorganism comprising any nucleic acid having any genetic modification that increases glucosamine-6-phosphate synthase activity or reduction of product inhibition of glucosamine-6-phosphate synthase activity, and the use of the claimed microorganism for the production of glucosamine. The claimed microorganism further contains any genetic modification of a list of enzymes recited in claim 57-60 and 68 and genetic modifications of a list of genes recited in claim 65.

The specification provides guidance and examples in substituting one amino acid at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 which is from *E. coli*. However, the specification does not provide guidance in making any microorganism comprising any genetic modification that increases glucosamine-6-phosphate synthase action; any genetic modification in a nucleic acid sequence encoding glucosamine-6-phosphate synthase; or an amino acid modification to the amino acid sequence of any glucosamine-6-phosphate synthase selected from the group consisting of deletion, insertion, inversion, substitution, and derivatization which results in increased glucosamine-6-phosphate synthase action. Furthermore, the specification does not provide guidance for any genetic modification of the list of enzymes recited in claim 57-60 and 68 and genetic modifications of the list of genes recited in claim 65.

The amount of experimentation to obtain the claimed microorganism for use in the production of glucosamine is undue because one skilled in the art would have to select a type of genetic modification out of a vast number of modifications to perform on the claimed microorganism, such as replacing the wild-type promoter of glucosamine-6-phosphate synthase with a high expression promoter, deleting, inserting, substituting, derivatizing, or combinations thereof to the nucleic acid encoding the amino acid sequence of glucosamine-6-phosphate synthase, or selecting proteins and enzymes other than glucosamine-6-phosphate synthase to genetically modify; expressing the glucosamine-6-phosphate synthase mutant, measuring the activity of said mutant; and determining whether the selected mutation results in an increase in glucosamine-6-phosphate synthase action. Applicants have not shown that any mutation in any protein or enzyme other than the mutation of glucosamine-6-phosphate synthase having the amino acid residue at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 replaced with another amino acid residue would result in a microorganism which has increased glucosamine-6-phosphate activity.

Since routine experimentation in the art does not include making a vast number of glucosamine-6-phosphate synthase mutants, and screening and selecting said mutants that have an increase in glucosamine-6-phosphate synthase action where the expectation of obtaining the desired mutation which results in an increase in glucosamine-6-phosphate synthase action is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as the specific type of genetic modification to perform on the specific proteins or enzymes

of claimed microorganism, the amino acid residues which can be modified that lead to the claimed effect, or the gene encoding the said synthase and its biological source. Without such a guidance, the experimentation left to those skilled in the art is undue.

Amending the claims to recite that the method uses a glucosamine-6-phosphate synthase having the amino acid residue at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 replaced with another amino acid residue where the glucosamine-6-phosphate synthase has increased activity compared to a wild-type glucosamine-6-phosphate synthase may overcome the rejection.

8. Claims 40-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 40-70 are genus claims that are directed toward any microorganism comprising any nucleic acid having any genetic modification that increases glucosamine-6-phosphate synthase activity or reduction of product inhibition of glucosamine-6-phosphate synthase activity, and the use of the claimed microorganism for the production of glucosamine. The scope of the claim includes many microorganisms and many glucosamine-6-phosphate synthases of any structure and amino acid sequence from any biological source, and the genus is highly variable because a significant number of structural differences between genus members is permitted.

The specification, however, only provides the following representative species encompassed by these genus claims: a glucosamine-6-phosphate synthase having the amino acid residue at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 replaced with another amino acid residue where the glucosamine-6-phosphate synthase has increased activity compared to a wild-type glucosamine-6-phosphate synthase. The specification fails to describe additional representative species of the claimed genus

Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Amending the claims to recite that the method uses a glucosamine-6-phosphate synthase having the amino acid residue at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 replaced with another amino acid residue where the glucosamine-6-phosphate synthase has increased activity compared to a wild-type glucosamine-6-phosphate synthase may overcome the rejection.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 40-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 40 (i), the phrase "encoding glucosamine-6-phosphate synthase which has glucosamine-6-phosphate synthase activity" is confusing since the nucleic acid encodes that enzyme and the nucleic acid itself does not have any enzymatic activiy. Claims 41-70 which depend from claim 40 are also rejected because they do not correct the defect of claim 40.

Claim Rejections - 35 U.S.C. § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 67 is rejected under 35 U.S.C. 102(b) as being anticipated by Dutka-Malen et al. Dutka-Malen et al. reference has been attached to the previous Office Action dated [7/20/00 (Paper No. 7)] and is not attached to the instant Office Action.

Dutka-Malen *et al.* make a genetically engineered *E.coli* host cell (see **Fig. 1**, p. 288) which is transformed with a recombinant vector containing the *E.coli* gene encoding glucosamine-6-phosphate synthase suitably linked to a *lac* promoter wherein said host cell overexpresses glucosamine-6-phosphate synthase as evident by an increase in enzyme activity. Glucosamine-6-phosphate synthase catalyzes the formation of glucosamine-6-phosphate. Genetic modifications include transformation of *E.coli* host cells with a recombinant vector containing a nucleic acid sequence which encodes glucosamine-6-phosphate synthase and overexpression of said synthase. Furthermore, linking the nucleic acid sequence encoding glucosamine-6-phosphate synthase to said *lac* promoter in said recombinant vector is a mutation to the glucosamine-6-phosphate synthase gene (*glms*).

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case the genetically engineered *E.coli* host cell taught by Dutka-Malen et al. meets the limitations of the claim since there is no structural difference between the claimed microorganism and the *E.coli* host cell taught by Dutka-Malen et al. Thus, the reference teachings anticipate the claimed invention.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

TEKCHAND SAIDHA
PRIMARY EXAMINER
3/15/04